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CASE REPORT

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The biker-glove pattern of congenital melanocytic nevi

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Abstract

Congenital melanocytic nevi (CMN) are common birthmarks with 20% occurring on the limbs. We describe 4 patients with acral CMN with a "biker-glove" distribution with sparing of the distal digits, as has previously been described in acral infantile hemangiomas (IH). The existence of the biker-glove pattern suggests that CMN arise from early mutations in melanocyte precursors and supports the recently described Kinsler-Larue hypothesis of mesenchymal distribution of melanocyte migration occurring in a circular field from a central point. Developmental errors in mesenchymal precursors with similar migration patterns may explain this shared pattern among CMN and IH.

1 | INTRODUCTION

Congenital melanocytic nevi (CMN) affect approximately 1% of newborns[1] and occur anywhere on the body.[2] In recent years, important advances have been made in the understanding of CMN pathogenesis. The causal mutations of the majority of CMN have been identified,[3-5] and recent data suggest the existence of two distinct melanocyte precursor populations leading to congenital pigmentary disease, implicating precursors derived from mesoderm in the patterning of most large CMN.[6]

A "biker-glove" pattern of acral infantile hemangiomas (IH) has been described, characterized by extension onto the fingers and toes with a contiguous border across digits and sparing of the distal tips.[7] This pattern did not correspond to known embryonic segments, sensory nerve distributions, dermatomes or lines of Blaschko. It was hypothesized that for the biker-glove pattern to arise, the developmental error giving rise to IH must occur between 38 and 52 days gestation, after the finger rays are formed but before the interweb spaces are completely developed and the distal digits have differentiated.[7]

We report 4 patients with biker-glove pattern of CMN. The existence of this pattern has important implications for our understanding of the origin and migration patterns of melanocytes and the cell of origin of CMN.

2 | PATIENT 1

A healthy 11-year-old girl has been followed since age 3 years for a medium-sized CMN (6 cm; M2 according to Krengel et al[8] classification, projected adult size 10 cm) of the right hand (Figure 1A-B). The light-to-medium brown thin plaque extended from the dorsal wrist to the base of the 2nd digit and to the distal interphalangeal (DIP) joint on the thumb, and around to the thenar eminence. Sparing of the distal fingertip, associated hypertrichosis, and slight dermal thickening was found. She has had no associated complications or treatment (Table 1).

3 | PATIENT 2

A 2-week-old girl presented with a large CMN of the right foot (circumferential, 8 cm in length; L1, projected adult size 22 cm) and multiple associated medium-sized and small satellite lesions (Figure 1C-D). The nevus extended onto each toe circumferentially with a contiguous line from one digit to the next and spared the tips of the digits. A brain and spine MRI did not demonstrate neurologic abnormalities. Her nevi have grown proportionally with her postnatal growth, without significant change in color, and she has not developed new satellites (Table 1).

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FIGURE 1 (A-B) Medium CMN of patient 1 extending from the dorsal hand and wrist to the thenar eminence and distally to the interphalangeal joint of the thumb, with sparing of the distal thumb. (C-D) Large CMN of the right lower leg and foot of patient 2 demonstrating a circular pattern with its central point on the dorsal foot and sparing of all distal digits

4 | PATIENT 3

A 3-year-old boy presented with a giant CMN of the left hand, arm, chest, and back with several satellites (G2, projected adult size > 60 cm). His course was complicated by severe dermatitis within the CMN, necessitating excision and grafting of much of the affected arm, and asymptomatic neurocutaneous melanosis. He died from melanoma arising in the central nervous system at age 11 years. Photographs taken before surgery of his arm reveal a giant nevus with sparing of the tips of all five fingers (Figure 2) (Table 1).

5 | PATIENT 4

A healthy 9-year-old girl was followed since age 1 year for a right 5th finger medium-sized CMN (3.5 cm circumferentially; M1, projected adult size 5 cm). Her CMN remained light brown and extended from the metacarpophalangeal (MCP) to the proximal interphalangeal (PIP) joints, starting dorsally and wrapping around nearly circumferentially to the ventral surface. Sparing of the distal fingertip was found. It had significant hypertrichosis and grew proportionally with her without complications (Table 1).

6 | DISCUSSION

Congenital melanocytic nevi (CMN) result from a single cell postzygotic mutation within presumed melanocytic precursor cells that divide and migrate to populate an area,[3,4,9] in these cases the distal limbs. All cases presented had sharp cut-offs and sparing of the distal extremity in a biker-glove pattern.

The biker-glove pattern suggests a specific timing of pathogenic events during fetal life, distinct populations of melanocytes and possibly the existence of protective factors within the digit tips. Upper limb development begins with the appearance of the limb bud on day 24; on day 38, finger rays develop and the interweb spaces begin to form by apoptosis. By day 52, fingers are well formed. For the biker-glove morphology to exist, the mutated melanocyte precursor must exist in the limb bud before the interweb spaces are completely developed.

To result in a larger nevus, such as the giant CMN in patient 3, the causal mutation is likely to occur in an earlier precursor cell, and conversely the medium-sized CMN in patient 4 must have resulted from a later mutation in a precursor that would populate only a small segment of the digit. Other genetic factors may also play a role in determination of final nevus size.

In 2018, Kinsler and Larue proposed that CMN arise from the mesoderm, from a population of melanocytes arising around the time of gastrulation, ultimately residing within the dermis.[6] The finding of a biker-glove pattern in CMN lends support to this hypothesis which also noted that melanocyte migration in most CMN emanates from a central point in a circular field, perhaps due to melanocyte precursor division and passive diffusion.[6] The patterns presented here correspond to the distal limb (or glove/stocking) field as described previously, with variable involvement of the digits and sparing of the finger/toe tips.[6]

Neither the segmental neural crest-derived melanocyte precursors nor the newly described mesoderm-derived melanocytes seem to supply the digital tips and nails.[6] It therefore follows that those structures are supplied by a yet unidentified population of melanocyte precursors. While it is also conceivable that the melanocyte precursors in the limb bud produce a digit tip and nail precursor very early on, the presence of fingertip sparing in giant CMN makes this unlikely.

It is noteworthy that CMN and IH both produce this same unique morphologic pattern on the extremities. The embryonic origins of IH remain unknown, in spite of much research. Multipotent dysregulated progenitor-like, hemangioma-derived stem cell (HemSC) proposed to give rise to IH do express mesenchymal markers (CD90).[10] Thus,

TABLE 1 Summary of cases

Patient #	Sex	Age at presentation	Affected limb	Distribution on limb	Color	Projected adult diameter	Clinical characteristics of nevus	Complications	Other cutaneous lesions	Additional medical history
1	F	3 y	Right upper extremity	Dorsal hand from wrist to base of 2nd digit, and extending onto thumb up to IP joint, thenar eminence	Light brown	10 cm (M2)	Speckled, became darker and less nodular over time, associated hypertrichosis	None	None	None
2	F	2 wk	Right lower extremity	Mid-calf to DIP on all fingers, primarily dorsal, wraps around ventrally with few islands of sparing on sole	Dark brown	22 cm (L1)	Thickened and became more uniformly dark brown over time	None	Numerous small and medium-sized satellites	Normal amniocentesis, normal brain and spine MRI
3	M	3 y	Left upper extremity	Entire arm from shoulder to fingertips circumferentially	Dark brown	>60 cm (G2)	Moderate color heterogeneity and rugosity, associated hypertrichosis	Severe dermatitis; Multiple reconstructive surgeries; Died of melanoma	Numerous small satellites	Neurocutaneous melanosis
4	F	1 y	Right upper extremity	D5 MCP to PIP, nearly circumferential wrapping from dorsal to ventral	Light brown	5 cm (M1)	Hypertrichotic	None	None	None

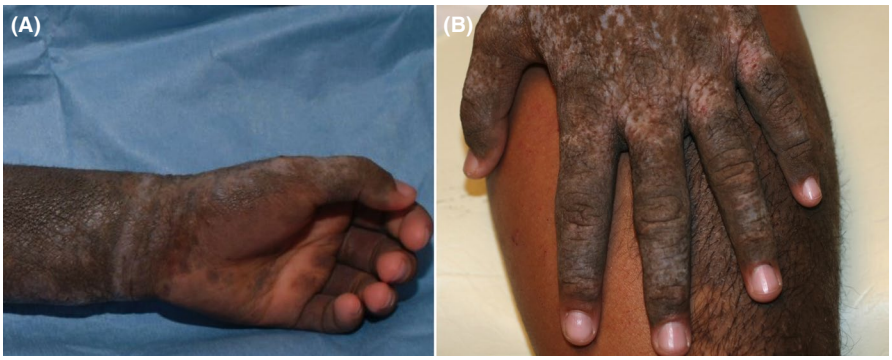

FIGURE 2 (A-B) Giant CMN of the left upper extremity of patient 3 demonstrating sparing of all fingertips

developmental errors in mesenchymal precursors with similar migration patterns may explain the shared biker-glove morphology between CMN and IH. Although controversial, reports of an association between CMN and IH could lend support to this theory.[11,12] When the biker-glove pattern was first described in IH, it was hypothesized that the event leading to this pattern would have to occur after the formation of finger rays but before the interweb spaces are completely developed.[7] The pathogenesis in CMN seems to differ slightly, in that an earlier causative event is hypothesized that still spares the distal digit because the distal digit is supplied by a separate, yet unidentified precursor.

Biker-glove nevi also represent an example of divided or kissing nevi, in which nevi involve adjacent mobile body parts that appear as a single nevus when those body parts are juxtaposed. Classically described as CMN on the upper and lower eyelids that appear as one lesion when the lids are closed,[13] divided CMN have also been described on the glans penis and adjacent foreskin[14] and divided epidermal nevi on adjacent fingers.[15] In all of these cases, the nevi are thought to initially arise as a single lesion at a time during embryogenesis before the two body parts separate.

The biker-glove pattern in CMN of the extremities suggests early mutations in melanocyte precursors and provides further support for the non-segmental migration pattern of some melanocyte precursors.[6] Recognition of morphologic patterns such as this may contribute to a greater understanding of melanocyte biology and the pathogenesis of CMN and IH.

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